

AMENDMENTS TO THE CLAIMS

1. (original) A method of preventing bone metastases comprising administering to a subject afflicted with metastatic cancer a therapeutically effective amount of a M-CSF mutein or mutein product thereby preventing bone loss associated with the metastatic cancer.
2. (original) A method of treating a subject afflicted with a metastatic cancer to bone comprising administering to said subject a therapeutically effective amount of a M-CSF mutein or mutein product thereby reducing the severity of bone loss associated with the metastatic cancer.
3. (original) The method according to claims 1 or 2 wherein said subject is a mammal.
4. (original) The method according to claim 3 wherein said mammal is human.
5. (original) The method according to claim 4 wherein said mutein or mutein product inhibits the interaction between M-CSF and its receptor (M-CSFR).
6. (original) The method according to claim 5 wherein said M-CSF mutein or mutein product inhibits osteoclast proliferation and/or differentiation induced by tumor cells.

7. (original) The method according to claim 5 wherein the metastatic cancer is breast, lung, renal, multiple myeloma, thyroid, prostate, adenocarcinoma, blood cell malignancies, including leukemia and lymphoma; head and neck cancers; gastrointestinal cancers, including stomach cancer, colon cancer, colorectal cancer, pancreatic cancer, liver cancer; malignancies of the female genital tract, including ovarian carcinoma, uterine endometrial cancers and cervical cancer; bladder cancer; brain cancer, including neuroblastoma; sarcoma, osteosarcoma; and skin cancer, including malignant melanoma or squamous cell cancer.

8. (original) A method of screening for a M-CSF mutein comprising the steps of:

a) contacting metastatic tumor cell medium, osteoclasts and a candidate M-CSF mutein or mutein product;

b) detecting osteoclast formation, proliferation and/or differentiation;
and

c) identifying said candidate as an M-CSF mutein or mutein product if a decrease in osteoclast formation, proliferation and/or differentiation is detected.

9. (original) The method of claim 8 wherein said metastatic tumor cell medium includes tumor cells.

10. (original) The method of claim 8 wherein said contacting step (a) occurs *in vivo*, said detecting step (b) comprises detecting size and/or number of bone metastases, and said candidate is identified as a M-CSF mutein or mutein product if a decrease in size and/or number of bone metastases is detected.

11. (original) The method of claim 8 further comprising the step of determining if said candidate M-CSF mutein or mutein product inhibits interaction between M-CSF and its receptor M-CSFR.

12. (original) A method of identifying a M-CSF mutein or mutein product that can prevent or treat metastatic cancer to bone, comprising the steps of:

(a) detecting binding of a candidate M-CSF mutein or mutein product to M-CSFR; and

(b) assaying the ability of said candidate M-CSF mutein or mutein product to prevent or treat metastatic cancer to bone *in vitro* or *in vivo*.

13. (original) A method of identifying a M-CSF mutein or mutein product that can prevent or treat metastatic cancer to bone, comprising the steps of:

(a) identifying a candidate M-CSF mutein or mutein product that inhibits the interaction between M-CSF and M-CSFR; and

(b) assaying the ability of said candidate M-CSF mutein or mutein product to prevent or treat metastatic cancer to bone *in vitro* or *in vivo*.

14. (original) A method of preventing bone metastases and tumor growth comprising administering to a subject afflicted with metastatic cancer therapeutically effective amounts of M-CSF mutein or mutein product and a therapeutic agent, thereby preventing bone loss associated with the metastatic cancer and preventing tumor growth.

15. (original) A method of treating a subject afflicted with a metastatic cancer comprising administering to said subject therapeutically effective amounts of M-CSF mutein or mutein product and a therapeutic agent, thereby reducing the severity of bone loss associated with the metastatic cancer and inhibiting tumor growth.

16. (original) The method according to claims 14 or 15 wherein said subject is a mammal.

17. (original) The method according to claim 16 wherein said mammal is human.

18. (original) The method according to claim 17 wherein said M-CSF mutein or mutein product inhibits the interaction between M-CSF and its receptor M-CSFR.

19. (original) The method according to claim 18 wherein said M-CSF mutein or mutein product inhibits osteoclast proliferation and/or differentiation induced by tumor cells.

20. (original) The methods according to claims 14 or 15 wherein the therapeutic agent is a bisphosphonate.

21. (original) The method according to claim 20 wherein the bisphosphate is zeledronate, pamidronate, clodronate, etidronate, tiludronate, alendronate, or ibandronate.

22. (original) The methods according to claims 14 or 15 wherein the therapeutic agent is a chemotherapeutic agent.

23. (original) The method according to claim 22 wherein the subject is precluded from receiving bisphosphonate treatment.

24. (original) The methods according to claims 14 or 15 wherein the M-CSF mutein or mutein product is effective to reduce the dosage of therapeutic agent required to achieve a therapeutic effect.

25. (original) The methods according to claims 14 or 15 further comprising the step of administering a non-M-CSF colony stimulating factor, for example G-CSF.

26. (original) A pharmaceutical composition comprising a M-CSF mutein or mutein product and a cancer therapeutic agent.

27. (original) A package, vial or container comprising a medicament comprising an M-CSF mutein or mutein product and instructions that the medicament should be used in combination with surgery or radiation therapy.

28. (original) A method of preventing or treating metastatic cancer to bone comprising the steps of administering a M-CSF mutein or mutein product to a subject and treating said subject with surgery or radiation therapy.

29. (original) A method of treating a subject suffering from a cancer, wherein the cells comprising said cancer do not secrete M-CSF, comprising the step of administering a M-CSF mutein or mutein product.

30.-64. (canceled)